Topics in
PAIN MANAGEMENT

Vol. 26, No. 11 | Current Concepts and Treatment Strategies | June 2011

CME ARTICLE

Review of Clinical Nerve Function Studies and Imaging: Part I

Clifford Gevirtz, MD, MPH

Learning Objectives: After participating in this activity, the physician should be better able to:

1. Use the time course in the development of new-onset nerve pathology to determine whether a lesion is acute or chronic.
2. Interpret the H-reflex test results to aid in diagnosis of S1 nerve root pathology.
3. Interpret the F-response test results to aid in the diagnosis of root pathology seen in plexopathy and radiculopathy.
4. Recognize 2 limitations in the performance of electromyography/nerve conduction velocity testing.

Introduction to Electrodiagnosis

Several procedures[1] are considered to be within the purview of "electrodiagnosis." These include electromyography (EMG), nerve conduction studies (including late potentials), and evoked potentials. These procedures are part of the fundamental work-up of cervical and lumbar radiculopathies. After completing this CME activity, pain practitioners should be better able to understand how to perform these tests, interpret the results, and evaluate their limitations.

In This Issue

CME Article: Review of Clinical Nerve Function Studies and Imaging: Part I 1

Ameritox to Pay $16.3 Million in Settlement Over Unnecessary Urine Drug Testing 7

Two More States—New Jersey and Maryland—Enact Medical Marijuana Legislation 9

CME Quiz 11

News in Brief 12

Electromyography

EMG[2] refers to the electrical recording of signals resulting from the depolarization of skeletal muscle. These signals may be measured from skin surface electrodes or needles placed within the body of the muscle. These 2 types of recordings are used for various purposes: needle recording is used to detect the behavior of individual muscle fibers and motor units, whereas surface recordings are used to detect muscle activity in particular positions or actions. Surface recording of EMGs is not the usual approach undertaken, although it may be of value in patients who are needle-phobic or cannot cooperate. Needle EMG is better able to determine whether there is damage to nerve fibers innervating individual muscles.

Needle EMG

Needle EMG records the amplitude and morphology of the electrical signals within skeletal muscle. Specific findings appear as a

Dr. Gevirtz is Associate Professor of Anesthesiology, Louisiana State University Health Center, New Orleans, LA 70112, and Medical Director, Somnia Pain Management, 627 W St, Harrison, NY 10528; E-mail: cliffgevirtzmd@yahoo.com.

All faculty and staff in a position to control the content of this CME activity and their spouses/life partners (if any) have disclosed that they have no financial relationships with, or financial interests in, any commercial companies pertaining to this educational activity.

Lippincott Continuing Medical Education Institute, Inc., is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Lippincott Continuing Medical Education Institute, Inc., designates this enduring material for a maximum of 1.5 *AMA PRA Category 1 Credits*™. Physicians should only claim credit commensurate with the extent of their participation in the activity. To earn CME credit, you must read the CME article and complete the quiz and evaluation assessment survey on the enclosed form, answering at least 70% of the quiz questions correctly. This activity expires on May 31, 2012.

result of myopathy and because of denervation of muscles. Some of these findings are seen spontaneously when simply recording from a needle-placed in the muscle, whereas others appear when the needle is moved within the muscle (insertional activity).

Surface recording of EMGs is not the usual approach; needle EMG is better able to determine whether there is damage to nerve fibers innervating individual muscles.

A normal muscle is generally electrically silent when recording is made from a needle electrode. The movement of the needle into the muscle normally elicits a brief burst of depolarization from the muscle fibers (termed insertional activity). This burst of activity ends immediately upon termination of the movement, with the return of electrical silence. The only place within the muscle that is not electrically silent is the motor end plate. There are 2 types of electrical activities that can be seen in the motor end plate at rest, namely: miniature end plate potentials and end plate spikes. The usual EMG examination will survey at least 10 locations within a single muscle before making a determination as to the normality of insertional activity or presence of abnormal activity at rest.

After the resting EMG and insertional activities are assessed, the patient is asked to contract the muscle. Normal contraction takes place during activation of motor neurons to the muscle,

The continuing education activity in *Topics in Pain Management* is intended for clinical and academic physicians from the specialties of anesthesiology, neurology, psychiatry, physical and rehabilitative medicine, and neurosurgery as well as residents in those fields and other practitioners interested in pain management.

Wolters Kluwer Health | Lippincott Williams & Wilkins

Topics in Pain Management (ISSN 0882-5646) is published monthly by Lippincott Williams & Wilkins, 16522 Hunters Green Parkway, Hagerstown, MD 21740-2116. **Customer Service: Phone (800) 638-3030, Fax (301) 223-2400, or Email customerservice@lww.com**. Visit our website at **lww.com.**

 Priority postage paid at Hagerstown, MD, and at additional mailing offices. GST registration number: 895524239. POSTMASTER: Send address changes to *Topics in Pain Management*, Subscription Dept., Lippincott Williams & Wilkins, P.O. Box 1600, 16522 Hunters Green Parkway, Hagerstown, MD 21740-2116.

Publisher: Randi Davis

Subscription rates: *Personal:* $256 US, $358.50 Foreign. *Institutional:* $492 US, $594.50 Foreign. *In-training:* $116 US, $144.50 Foreign. *Single copies:* $49. Send bulk pricing requests to Publisher.

Topics in Pain Management is indexed by SIIC (Sociedad Iberoamericana de Información Científica).

each of which is connected to many muscle fibers scattered throughout the muscle (denoted as a motor unit). The electrical signal that is recorded as a "motor unit potential" (MUP) is derived from the integration of the electrical signals from the discharge of several muscle fibers that are attached to the same motor neuron and are within recording distance of the tip of the sensing needle (1–3 mm). The amplitude of the MUP is dependent on the density of the muscle fibers attached to that one motor neuron. For most clinically tested muscles, the amplitude is between 200 and 2000 μV. It is also important to note that MUPs usually have only 1 or 2 upward peaks. As the strength of contraction is slowly increased, motor units are recruited in an orderly sequence. Each active motor unit increases its firing frequency to around 10 Hz, at which point an additional motor unit is recruited. This process is quite orderly and can be quantified as a "recruitment pattern."

Needle EMG evaluates the integrity of the motor unit, that is, the motor neuron, motor axon, and the muscle to which it is attached.

Delayed recruitment (defined as increased firing rates of individual MUPs before the recruitment of an additional unit) is a reflection of loss of motor units within the muscle. The final step in the EMG assessment of a muscle involves asking the patient to maximally contract the muscle. During such contraction, the electrical activity should fully obscure the baseline (defined as a full interference pattern). An incomplete interference pattern is considered to be a reflection of loss of motor units in a muscle, although it can also be seen with diminished voluntary effort, that is, someone not fully cooperating with the examiner.

Needle EMG evaluates the integrity of the motor unit, that is, the motor neuron, motor axon, and the muscle to which it is attached. Myopathies can produce some membrane instability if the disease is active. This can result in the appearance of "fibrillation potentials" that represent the contraction of individual muscle fibers.

Muscle disease causes change within the motor unit. Because muscle fibers are not functioning well in myopathy, the MUPs tend to be of low amplitude short duration. During even a minimal contraction, a greater number of these muscle fibers are needed to maintain the force of contraction, so "early recruitment" of motor units is seen (more motor units firing at higher rate than expected for the force).

Fibrillations and positive sharp waves are the most reliable and objective findings for damage to motor axons to the muscle after 1 week, and these may last up to 12 months after the initial event.

Editor's Note:

The American Board of Anesthesiology Pain Medicine curriculum covers several areas of diagnostic testing. With respect to clinical nerve function studies and imaging, the key topics are delineated by the curriculum as follows:

Clinical Nerve Function Studies and Imaging

02.09.01 Electrical nerve stimulation (EMG/NCV/evoked potentials): uses and limitations
02.09.02 Laser-evoked potentials: uses
02.09.03 Quantitative sensory testing: uses and limitations
02.09.04 Skin punch biopsy: assessment of innervation density
02.09.05 MRI, fMRI, and MR spectroscopy: uses
02.09.06 PET scans: uses
02.09.07 EEG, MEG: uses

We will cover EMG/NCV and laser-evoked potentials in part I, and the remainder in part II.

Damage to motor axons (either at the level of the anterior horn cell, the motor root, or at the peripheral nerve) results in a distinct series of quantifiable changes in the EMG. These changes are triggered by disruption of the motor axon, and they develop in an orderly sequence that can help determine the actual timing of the injury. These changes are not seen with damage to the myelin of the motor axon (assuming that the axon, itself, is undamaged). It is interesting that although damage to myelin can result in complete block of motor conduction and even produce complete paralysis of the muscle, there are no changes associated with denervation. Similarly, damage to the central nervous system above the level of the motor neuron (such as by spinal cord injury or stroke) can result in complete paralysis without any abnormality on needle EMG, with the exception of an incomplete or absent interference pattern.

The timing of an injury can be placed from 1 week to 1 year by reviewing the recording for acute injury.

When a muscle becomes denervated, changes within muscle fibers can be detected as abnormal electrical signals. Within the first week or two, the denervated muscle fiber becomes progressively more irritable. Electrical discharges provoked by movement of the needle can outlast the actual movement by more than a second. This is termed "increased insertional activity." Although this finding is not specific, it does indicate that the muscle is excessively irritable. The muscle fibers also become increasingly chemically sensitive to their microenvironment and their membranes can also become unstable enough to produce abnormal spontaneous activity. This is recorded as depolarization of individual muscle fibers.

The spontaneous depolarizations of the individual fibers appear as fibrillation potentials and positive sharp waves. These do not occur in normal muscles, because the normal muscle

fibers are responsive to the activation of their motor unit only by normal neuromuscular transmission.

It takes more than a week for such potentials to develop, and they will then disappear with complete degeneration of the denervated muscle fiber.

Fibrillations and positive sharp waves are the most reliable and objective findings for damage to motor axons to the muscle after 1 week, and these may last up to 12 months after the initial event.

If there is ongoing damage from pathology, such as in amyotrophic lateral sclerosis, there will be ongoing denervation. The finding of fibrillations and positive sharp waves is often termed "acute denervation," but the "acute" in this case refers to weeks and months.

In sum, the timing of an injury can be placed from 1 week to 1 year by reviewing the recording for acute injury. If, for example a patient claims to have been injured by a strong paresthesia during placement of block, an EMG taken immediately after should not show fibrillation potentials and positive sharp waves. Similarly, if there is a baseline EMG conducted before a nerve block that is unchanged afterward, then any deficit is preexisting.

The typical needle EMG examination requires sampling several muscles.

Reinnervation of muscle is an ongoing process, occurring whenever a muscle is partially denervated. This process typically involves the development of sprouts from adjacent, unaffected motor nerve fibers that ultimately contact at least some of the denervated muscle fibers. These reinnervated muscle fibers group right in the area of other, normally innervated muscle fibers. This process results in the development of groups of reinnervated muscle fibers attached to individual motor neurons. Typically, these motor units become significantly larger both in amplitude and duration because the needle is to be recording from more muscle fibers within this group. In addition, the MUPs often become more irregular (termed "polyphasic"). This process takes months to develop and indicates the presence of chronic denervation.

The typical needle EMG examination requires sampling several muscles. Its ability to localize a lesion depends on sampling muscles innervated by the same nerve but different nerve roots, muscles innervated by the same nerve root but different nerves, and muscles innervated at various locations along the course of the nerves. Paraspinal muscles can be very useful in this regard because nerve root damage will tend to produce abnormalities in these muscles and within the muscles of the limbs. As an example, this can help distinguish a radiculopathy from a plexopathy or peripheral neuropathy. Sometimes precise localization can be difficult due to the overlap in innervation of the various nerve root levels or normal anatomic variation.

NCV Studies

Nerve conduction studies can test sensory and motor nerve fibers but not sympathetic fibers. Nerve conduction velocity (NCV) serves to determine both the speed of conduction and the amplitude of the electrical signal evoked after stimulation of a nerve. It can detect areas of focal nerve damage.

Motor Conduction Studies

Motor conduction studies[3] are performed by stimulating a motor nerve while monitoring the response from its target muscles. It is important to recognize that the electrical signal being recorded after motor nerve stimulation [called the compound muscle action potential (CMAP)] is actually generated by the muscle, and therefore it is quite large. When motor nerve fibers are stimulated close to the muscle, the amount of time before the muscle starts depolarizing is called the "terminal latency."

Terminal latency includes both the amount of time it takes the nerve to conduct from the point of stimulation to the motor end plate area and for the neuromuscular junction transmission to activate the muscle.

The term "latency" in electrodiagnosis is used to define the time between a stimulus and the appearance of a response. In the case of terminal latency, this value includes both the amount of time it takes the nerve to conduct from the point of stimulation to the motor end plate area and the amount of time for the neuromuscular junction transmission to activate the muscle.

There are tables of normal values for the terminal latencies of defined lengths for each of the main motor nerves. Abnormal prolongation of this value helps in the detection of distal entrapment neuropathies. Once a terminal latency has been recorded, the motor conduction velocity can be determined by stimulation of another, more proximal site along the motor nerve.

Compared with motor conduction, sensory conduction velocity is an easier measurement to compute but is more technically difficult to record.

The computation of motor NCV requires knowing the precise distance between the 2 simulation sites and the difference in the terminal latencies recorded from the more distal and more proximal sites. Dividing the distance by the time gives the NCV over the segment in between the stimulus points.

Sensory Conduction Studies

Compared with motor conduction, sensory conduction velocity is an easier measurement to compute but is more technically

difficult to record. This test can be done in either an orthodromic direction (ie, distal stimulation and proximal recording) or antidromic direction (ie, proximal stimulation and distal recording). The sensory nerves that can be recorded[4] are radial, median, ulnar, sural, and superficial peroneal. The recording is made directly from the sensory nerve [the evoked response is called the sensory nerve action potential (SNAP)] and therefore is quite small (about a thousand times smaller than the CMAP). The distance between the site of stimulation and recording is divided by the latency (ie, the amount of time from the electrical stimulus to the SNAP) to determine the sensory NCV over the segment.

Measuring NCV results

The results of nerve conduction studies are compared with tables of normal values and also with the values in an unaffected limb of the same individual. There are normal values for both sensory and motor conductions and for terminal latency. For example, a good rule of thumb is that motor nerve conduction should be at least 40 m/s in the lower limb, whereas sensory conduction should be at least 40 m/s. It is very important to recognize that normal aging can slow the conduction velocity, as can low temperature of a limb. In the very elderly, it may be very difficult to record the sural SNAP. There are tables that can be used to adjust normal values for extremes of age. For the F-response, there are also tables that account for height.

The two values that are most important in a nerve conduction study are the speed of conduction and the amplitude of response.

The 2 values that are most important in a nerve conduction study are the speed of conduction and the amplitude of response. The speed is a reflection of the diameter of the axons and, most importantly, the thickness of the myelin sheath. Most of the conditions that damage nerves result in at least some injury to the myelin covering the axons. During recovery from focal neuropathy, a thinner and less well-developed myelin sheath is produced, slowing conduction. Of course, this slowing would be greatest in the area of the original damage. In addition, other conditions such as Charcot-Marie-Tooth disease or Guillain-Barré syndrome preferentially damage the myelin of the largest, fastest conducting fibers. This causes slowing, which manifests by decreased conduction velocity. Actual blockage of conduction can occur because of damage to the myelin of 3 or 4 internodal segments. When remyelination does occur, conduction velocity is still decreased to the shorter internodal distance.

Axonal neuropathies can occur in toxic neuropathies (eg heavy metals, chemotherapy). In these situations the amplitude of the CMAP and SNAP are much more affected than velocity. Diabetic distal symmetrical neuropathy, the most common neuropathy, has features of both demyelination and axonal damage.

Understanding Late Potentials

Late potentials are electrodiagnostically elicited responses in muscle that appear more than 10 to 20 milliseconds after stimulation of motor nerves. They have been termed "late potentials" because they take substantially longer to appear than the direct responses to stimulation of motor nerves. There are 2 distinct types of late responses, the H-reflex and the F-response.

The H-Reflex

The first type of late response, the H-reflex, was named in the honor of Hoffmann,[5] who first described this response in 1918. The pathway for this reflex and the significance of abnormalities are easiest to understand by recognizing that it is basically the electrophysiologic equivalent of the muscle stretch reflex. The H-reflex is most commonly tested by electrical stimulation of the tibial nerve, with recordings from the gastrocnemius and soleus muscles. Therefore, this response uses the same neural pathway as the ankle-jerk reflex.

In practical terms, only the gastrocnemius and soleus muscles produce H-reflexes that are reliable enough to be clinically useful.

Understanding of the H-reflex is aided by some knowledge of the technical details of the procedure.[6] Electrical stimulation will depolarize the largest, most heavily myelinated nerve fibers at a lower stimulus intensity than is required to activate other smaller nerve fibers. Because the largest nerve fibers in a peripheral nerve are those arising from muscle stretch receptors, there should be a stimulus intensity that activates muscle stretch afferent nerve fibers without directly activating many motor nerve axons (which are slightly smaller in diameter).

When muscle stretch sensory fibers are stimulated, a monosynaptic reflex contraction will be elicited in the muscle. Because this response must travel the sensory axon all the way back to the spinal cord before synapsing on the motor neuron in the anterior horn, and the motor response must then travel the length of the motor axon to reach back to the muscles, this reflex takes a relatively long time. That is where the designation of "late potential" originates.

In theory, this reflex can be elicited from virtually any muscle. However, in practical terms, only the gastrocnemius and soleus muscles produce H-reflexes that are reliable enough to be clinically useful. Therefore, when a clinical electrodiagnostic procedure reports an H-reflex, the test has evaluated the integrity of the reflex arc from the tibial nerve through the spinal cord and back to the gastrocnemius and soleus muscles.

Damage to any portion of the reflex arc, including the sciatic nerve or the S1 sensory or motor nerve root, can result in loss or slowing of the reflex response. Because the H-reflex is mediated primarily over the S1 nerve root (just like the ankle-jerk reflex), it is a sensitive test for S1 radiculopathy.

Although the H-reflex may be viewed as an electrical test of the ankle jerk, or Achilles tendon reflex, there are some differences that should be noted. For example, as opposed to the clinical ankle jerk, the H-reflex can be precisely quantified (in both latency and amplitude) and, therefore, may be a more useful index to follow with time or treatment. In addition, the H-reflex can be elicited from many patients even when the ankle jerk cannot be elicited because of age.

With the notable exception of the gastrocnemius and soleus muscles, the H reflex is very difficult to elicit. This limits the H-reflex to being a sensitive, specific, and quantitative test of sciatic nerve and S1 nerve root function. This may be of use in investigating patients with suspected S1 radiculopathy.

The F-Response

The second type of late potential is the F-response.[7] This is a response that occurs in muscles during a motor nerve conduction study long after the initial contraction of the muscle (the CMAP). Although the CMAP usually appears within several milliseconds (depending on how close the stimulus point is to the muscle), depending on the stimulus site, another response can be normally recorded in the muscle approximately 25 to 55 milliseconds later. Because this response was first recorded in foot muscles, it came to be known as the F-response.

Because the F-response traverses more proximal portions of the motor axons, it may be useful in the investigation of proximal nerve pathology, such as root pathology seen in plexopathy, radiculopathy, Guillain-Barré syndrome; chronic inflammatory demyelinating polyradiculopathy; and demyelinative peripheral neuropathies.

Over time, it was determined that this late response was not a reflex in the usual definition. The electrical impulse is transmitted proximally along the motor axon from the site of initiation of the action potential. When this antidromic (opposite to the normal direction of conduction) depolarization reaches the motor neurons in the spinal cord, a percentage of these motor neurons are activated a second time. This results in an orthodromic electrical signal being conducted in the normal (orthodromic) direction from the spinal cord to the muscles innervated by the nerve.

This second, later activation produces a small muscle contraction, the F-response. Because the number of motor neurons that are reactivated is somewhat unpredictable, the amplitude of this signal is variable and, therefore, amplitude measurements are usually not used. However, delay in the F-response indicates some slowing of conduction of the motor axon.

Because the F-response traverses more proximal portions of the motor axons, it may be useful in the investigation of proximal nerve pathology, such as root pathology seen in plexopathy, radiculopathy, Guillain-Barré syndrome, or chronic inflammatory demyelinating polyradiculopathy (CIDP).

The F-response is also very helpful in the confirmation of demyelinative peripheral neuropathies. In these neuropathies the F-responses may be quite prolonged.

Electrodiagnostic Tests of Peripheral Nerve Function

Nerve Conduction

Motor and sensory nerve conductions can be determined from peripheral nerves superficial enough to be stimulated transcutaneously. The muscle action potential is recorded from the overlying surface, the median nerve is stimulated transcutaneously at a measured distance from the recording electrode (point A), and the latency (time from stimulus to response) is recorded. Similarly, the latency from stimulating the nerve at another point (point B) is determined.

Latency A minus latency B represents the time it takes for the nerve impulse to travel from A to B. The distance from A to B divided by this time is the measured conduction velocity. The NCV will be normal (about 40–70 m(s) as long as there are some fast-conducting fibers left in the nerve. It is important to note that normal nerve conduction does not, therefore, rule out a peripheral neuropathy.

Although most pain practitioners use EMG/NCV testing in evaluation of lumbar radiculopathy, an underused indication is evaluation of complex regional pain syndrome.

Demyelinating neuropathies produce marked slowing of the nerve conduction. Axonal neuropathies may produce some increase in distal latency, but usually the nerve conductions are normal or only slightly reduced. Focal slowing may be detected in cases of nerve compression, which as a rule initially causes a demyelinating lesion.

Sensory nerve conductions are determined by stimulating the skin and recording from the appropriate nerve. The potential recorded is very small, and consequently very mild nerve injuries alter or abolish it.

Clinical Application

Although most pain practitioners use EMG/NCV testing in evaluation of lumbar radiculopathy, an underused indication is evaluation of complex regional pain syndrome (CRPS).

Bruehl et al[8] reviewed evidence supporting the clinical lore of 3 sequential stages of CRPS and analyzed the characteristics of possible CRPS subtypes. In a series of 113 patients who met International Association for the Study of Pain criteria for CRPS, the patients underwent standardized history and physical examinations to assess CRPS signs and symptoms in 4 domains identified in previous research, as follows: pain/sensory abnormalities, vasomotor dysfunction, edema/sudomotor dysfunction, and motor/trophic changes.

K-means cluster analysis was used to derive 3 relatively homogeneous CRPS patient subgroups based on similarity of sign/symptom patterns in these domains. The authors documented that the resulting CRPS subgroups did not differ significantly regarding pain duration, as might be expected in a sequential staging model.

However, the derived subgroups were statistically distinct, and suggested 3 possible CRPS subtypes: (1) a relatively limited syndrome with vasomotor signs predominating; (2) a relatively limited syndrome with neuropathic pain/sensory abnormalities predominating; and (3) a florid CRPS syndrome similar to "classic reflex sympathetic dystrophy" descriptions, referring to a type of CRPS—CRPS type 1—that is also called reflex sympathetic dystrophy. Subtype 3 showed the highest levels of motor/trophic signs and possible disuse-related changes (osteopenia) on bone scan, despite having directionally the briefest pain duration of the 3 groups. Importantly, they concluded that EMG/NCV testing identifies subtype 2 as equivalent to CRPS type 2 (causalgia). Overall, these results are consistent with limited previous work that argues against 3 sequential stages of CRPS.

Conclusion

NCV and EMG studies are the mainstay of electrodiagnosis. It is important for pain practitioners to recognize their use in confirming diagnosis and serving as a tool to determine timing of injury. This is especially important in dealing with litigious patients who seek to blame nerve blocks on their worsening condition. Specifically, if there is severe preexisting neuropathy, then it is unlikely that a properly performed nerve block made the condition worse.

After completing this CME activity, pain practitioners should be better able to utilize the time course in the development of new-onset nerve pathology to determine whether a lesion is acute or chronic, evaluate the H-reflex test results to aid in the diagnosis of S1 nerve root pathology, assess the F-response test to assist in the diagnosis of root pathology seen in plexopathy and radiculopathy, and interpret two limitations in the performance of EMG/NCV testing. ■

References

1. American Association of Electromyography and Electrodiagnosis. Guidelines in electrodiagnostic medicine: Rochester MN. *Muscle Nerve*. 1992;15(2):229-253.
2. Magladary JW, McDougal DB. Electrophysiological studies of nerve and reflex activity in normal man. *Bull Johns Hopkins Hospital*. 1950;86:265-269.
3. Felsenthal G. Median and ulnar motor and sensory latencies in the same normal subject. *Arch Phys Med Rehabil*. 1977;58:297-301.
4. Pappagallo M. Chapter 29: Neuropathic pain in peripheral neuropathies. *Practical Pain Management*. 3rd ed. In: Tollison CD, Satterthwaite JR, Tollison JW, eds. Philadelphia, PA: Lippincott Williams & Wilkins; 2002:431-447.
5. Hoffmann P. Uber die Beziehungen der Sehnenreflexe zur willkfirlichen Bewegung und zum Tonus. *Z Biol*. 1918;68:351-356.
6. Hugon M. Methodology of the Hoffman reflex in man. In: Desmedt JE, ed. *New Development in Electromyography and Chemical Neurophysiology*. Basel, Switzerland: Karger; 1973:277-293.
7. Yates SF, Brown WF. Characteristics of the F response: a single motor unit study. *J Neurol Neurosurg Psychiatry*. 1979;42:161-170.
8. Bruehl S, Harden RN, Galer BS, et al. Complex regional pain syndrome: are there distinct subtypes and sequential stages of the syndrome? *Pain*. 2002;95(1-2):119-124.

Ameritox to Pay $16.3 Million in Settlement Over Unnecessary Urine Drug Testing

The law is clear: Patient testing by private laboratories requires strict accountability—an unbroken chain of records, data, claims, payments, statements, and results.

On the physician's side, the law requires honesty and transparency when it comes to test authorizations, payment for services, and the interpretation of said results. Anything less will cast a suspicious shadow—or worse, as some physicians who dealt with Ameritox have learned the hard way.

A recent case involving Ameritox, a Baltimore-based drug testing company whose primary laboratory is in Midland, Texas, shows how it can all go wrong—and how one ethically minded person can make it right again by leveraging the clarity of the law.

A former Ameritox sales representative filed suit against the company in 2007 under the False Claims Act.

According to the allegations, Ameritox was paying doctors in pain-management practices to prescribe medically unnecessary drug tests, to be paid for by Medicare. Not only were the doctors ordering tests that were not necessary, Ameritox employees were working in these same offices and sending off urine samples to the laboratory whether doctors wanted them to or not, according to the allegations.

The Ameritox case resulted in the company agreeing to pay a $16.3 million settlement, announced last November by the US Department of Justice. The scheme became known after a former Ameritox sales representative, Debra Maul, filed suit against the company in 2007 under the False Claims Act. The act permits private citizens with knowledge of fraud to sue a company on behalf of the United States, and to share in any recovery. Maul received $3.4 million from the federal share of the settlement.

According to the Department of Justice, a number of pain management physicians who prescribe narcotics to their patients received kickbacks from Ameritox for prescribing unnecessary tests for these patients. The settlement resolves allegations that Ameritox made cash payments to its physician clients from 2003 through 2006 to induce the referral of drug-testing services, according to a press release from the US Attorney Robert E. O'Neill, Middle District of Florida. The press release was posted online by the *Tampa Bay Business Journal*.

The settlement also resolves claims arising from the offer by Ameritox of free collector personnel to its physician clientele from January 1, 2003, through June 30, 2010, to induce the referral of Medicare business, according to the press release. Of the total settlement amount, the federal government will receive $15,486,000, with the balance of $814,000 to be split among various states.

"The drug test measures the quantity and quality of medications in the patients' systems and helps physicians determine whether their patients are being compliant in taking the medications," the Department of Justice said in announcing the settlement. "The tests also assist in identifying patients who are at risk of diverting their medications."

Testing done under false pretenses can exact a devastating toll on the patient—and, as in the Ameritox case, it can prove embarrassing for the physician as well.

Typically, some patients who are prescribed narcotics are compelled to undergo drug tests to ensure that they are taking the medication as prescribed. The results of these tests can affect the patient's employment, his or her personal life, and, of course, decisions about the continued use of the prescribed medication. Testing done under false pretenses, then, can exact a devastating toll on the patient—and, as in the Ameritox case, it can prove embarrassing for the physician as well.

The Ameritox settlement resolved claims that the company not only made cash payments to physicians, but that it also offered test-collection personnel to physicians "in order to induce the referral of Medicare business," according to the Department of Justice.

In addition to the financial settlement, Ameritox agreed to enter into a 5-year corporate integrity agreement with the Department of Health and Human Services (HHS) Office of the Inspector General. The agreement will entail an independent review of the organization to oversee its contractual dealings.

"Financial kickbacks can subvert the medical decision-making process resulting in abuse of government health programs and harm to the beneficiaries of those programs," said Daniel R. Levinson, HHS Inspector General.

Maul's attorney, David Linesch, told the *St. Petersburg Times*, "She just believes in doing it the right way and couldn't work at a place that didn't."

The lawsuit is United States ex rel. Maul *v*. Ameritox, Ltd., case no. 8:07-cv-953-T-26EAJ (MD Fla.).

Maul is now a vice president for sales at another laboratory company.

According to its Web site, Ameritox is currently building a second laboratory in Greensboro, North Carolina.

Laboratory Was Subject of Controversy For Years

Even before the justice department case and settlement, Ameritox was no stranger to controversy. On www.cafepharma.com, a Web site where pharma and medical sales industry insiders are able to post questions and comments anonymously, Ameritox received searing attacks and staunch defenses and testimonials, dated before the case was made public.

The attacks generally said that the sales staff is pushed too hard and in turn can come on strong to physicians, who are afraid of both losing patients because of increased testing and being prosecuted if patients are found to be abusing or diverting narcotics.

Defenders accused the attackers of being among the low-performing staff who took advantage of the "low-hanging fruit" in the early days of the urine toxicology screening increase, before other companies began competing in the field. They said the company was ethical and had good compensation packages, and that the company eats the cost of many bills if the patient is not insured.

In some cases, attackers countered by asking if the poster was from Ameritox management—or on drugs, perhaps. Several of those who posted disclosed that they did, in fact, currently work for Ameritox, although their posts were anonymous. ■

Two More States—New Jersey and Maryland—Enact Medical Marijuana Legislation

New Jersey and Maryland are the latest states to approve the use of medical marijuana, with laws that have far more restrictions on patients who use the drug for nausea, pain, and multiple sclerosis symptoms.

New Jersey's statute, though seen by advocates as too restrictive, is expected to result in medically prescribed use of cannabis starting this summer, making it the 16th state (including the District of Columbia) to proffer regulated use of the drug. Meanwhile, physicians are seeking guidance on how to meet their patients' needs while staying on the right side of the law.

In federal law terms, there is no such thing as "medical marijuana." There is just "marijuana," and it is not legal to grow, sell, possess, or consume it under federal law.

One thing is clear: In federal law terms, there is no such thing as "medical marijuana." There is just "marijuana," and it is not legal to grow, sell, possess, or consume it under federal law. US Supreme Court decisions have upheld that.

In Gonzales *v* Raich (previously Ashcroft *v* Raich), 545 US 1 (2005), the US Supreme Court ruled that under the commerce clause of the US Constitution, the US Congress may criminalize the production and use of home-grown cannabis although states approve its use for medicinal purposes.

Even as states push their own legal and ethical boundaries regarding individuals' use of the drug for medical purposes, the federal government maintains that marijuana is illegal. However, the Obama administration, unlike the Bush administration, has not actively sought to prosecute those growing or using marijuana for medical needs in states where it is legal to do so.

Still, federal government Web sites are sharply critical of those who claim the drug can benefit patients suffering from chronic problems. For example, here is the White House Office of National Drug Control Policy (NDCP) statement on medical marijuana—part of a list of talking points under the title "'Medical' Marijuana—The Facts":

"There are no FDA-approved medications that are smoked. For one thing, smoking is generally a poor way to deliver medicine. It is difficult to administer safe, regulated dosages of medicines in smoked form. Secondly, the harmful chemicals and carcinogens that are byproducts of smoking create entirely new health problems. There are four times the level of tar in a marijuana cigarette, for example, than in a tobacco cigarette…."

The NDCP statement offers some encouragement about a drug, Marinol, which uses synthesized tetrahydrocannabinol—the "active ingredient" in marijuana. The drug, as prescribed by physicians, can relieve nausea associated with chemotherapy and loss of appetite experienced by AIDS patients.

"The most comprehensive, scientifically rigorous review of studies of smoked marijuana was conducted by the Institute of Medicine, an organization chartered by the National Academy of Sciences," the fact sheet says. "In a report released in 1999, the Institute did not recommend the use of smoked marijuana, but did conclude that active ingredients in marijuana could be isolated and developed into a variety of pharmaceuticals, such as Marinol. In the meantime, the DEA is working with pain management groups, such as Last Acts, to make sure that those who need access to safe, effective pain medication can get the best medication available."

The federal stance is not only critical of the use of marijuana as a prescribed medicine but also in the consideration of the drug as anything but an illicit substance that is harmful in all forms. For every claim of its efficacy as a pain and nausea reliever, the federal government imparts a counter claim that should be familiar to most Americans in the decades-old "war on drugs" environment:

"Marijuana use is associated with dependence, respiratory and mental illness, poor motor performance, and impaired cognitive and immune system functioning, among other negative effects," the NDCP states. "Marijuana is the most commonly used illicit drug in the United States, with nearly 17 million Americans age 12 and older reporting past-month use, and 374,000 people entering an emergency room annually with a primary marijuana problem."

The position also captures the economics of the drug becoming legal—something not normally germane to a debate about a given drug's effectiveness, but here it could be seen as an essential part of the conversation: The threshold fact about marijuana is that it remains illegal and illicit in the majority of instances.

"[B] because drug use is sensitive to price, especially among young people, higher prices help keep use rates relatively low," the NDCP states, making note of a RAND Corporation study, "Altered State," which predicts that if marijuana was legalized, its price would plummet and therefore use of the drug would rise. The example of OxyContin is also spotlighted, with the argument that although that drug is closely regulated, the fact that it is legal has made it easier to obtain and, therefore, easier to abuse.

Despite these arguments and many more, a number of states are moving ahead with a legal regimen that enables doctors to access legally grown and distributed marijuana for patient use. California seems to be the most permissive of these regimens: that state's law, according to the *Associated Press*, allows patients suffering from a wide range of ailments to grow their own marijuana or get it with a doctor's "recommendation" from a dispensary operated as a nonprofit collective. California voters approved this law in 1996—years ahead of other states. A topic of consistent concern in that state, however, is how local communities can deal with the problems associated with the dispensaries. Some cities and towns have banned them completely, whereas others do nothing. Many communities have local ordinances to keep public behavior associated with the dispensaries

in check—there are not many opportunities to start a "little Amsterdam," even in California.

The federal government's position on California's law, and that of other states with their own medical marijuana guidelines on the books, seems to be relatively simple: "look the other way." The common ground between the Drug Enforcement Administration and the states seems to be a focus on who can access the drug, who can cultivate it, and how much of it a person can have in their possession at any given time. Perhaps this is where the medical community, especially those who are tasked with providing relief from pain due to chronic illness, can have a great deal of influence.

"There is ample evidence that marijuana does offer some relief more effectively than conventional medications to some patients who suffer from some serious ailments, including multiple sclerosis, AIDS, and cancer," the *San Diego Union-Tribune* said in a March 27, 2011 editorial concerning 2 proposed city ordinances that would address parts of the law as it pertains to dispensaries, such as limiting them to locations in specific industrial and commercial zones.

Although this editorial acknowledges the efficacy of the drug, it also asserts that, at least in San Diego, the dispensaries have created "a serious community problem." It endorses the proposed ordinances, which also would require employee background checks, effective security measures, regulated hours, and other advancements to ensure that marijuana is only going to those for whom doctors intend.

So at least in California, there seems to be a turn toward a new kind of progressivism about medical marijuana—one that inculcates the federal position that the drug is, by its very nature, addictive and, therefore, requires close monitoring if it is to be safe, effective, and, in turn, medically useful.

Some would argue that New Jersey's law, though more restrictive, will help that state avoid some of California's problems. It requires doctors to register with the state if they plan to prescribe the drug, and they must demonstrate that other treatment regimens have been tried without success before marijuana is introduced. Patients also must register (with both their doctor and the state), pay a $200 fee, and receive the drug only from authorized organizations. They cannot grow the drug at home, or buy it from a dealer with a "doctor's note."

The other 14 states (including the District of Columbia) have laws that permit medical marijuana to one degree or another. Other states, such as Pennsylvania, are considering their own laws. Right now, New Jersey's model seems to be popular among lawmakers in these "leaning" states.

What Do the New Laws Mean for Physicians?

What do all of these laws, regulations, and ordinances mean for the professional community associated with pain relief? Physicians usually are not fond of case-by-case solutions to human problems, so, predictably, the American Medical Association (AMA) urges the government to rely on the science more than the politics:

"Results of short-term controlled trials indicate that smoked cannabis reduces neuropathic pain, improves appetite and caloric intake especially in patients with reduced muscle mass, and may relieve spasticity and pain in patients with multiple sclerosis," the organization said in late 2009, when it declared its support of the drug in a health care setting. "However, the patchwork of state-based systems that [has] been established … is woefully inadequate in establishing even rudimentary safeguards that normally would be applied to the appropriate clinical use of psychoactive substances. The future of cannabinoi0d medicine lies in the rapidly evolving field of botanical drug substance development, as well as the design of molecules that target various aspects of the endocannabinoid system. To the extent that rescheduling marijuana out of Schedule I will benefit this effort, such a move can be supported."

In this case, the science seems to be "in." As a consequence, many doctors are moving forward along with the AMA's position. At the same time, they have to consider the cognitive dissonance between what their state and federal governments are saying, and act accordingly. In this gap, lobbyists, researchers, ethicists, and a host of other experts are establishing a future in which cannabis can become part of the conversation in the doctor's office—rather than the alley down the street. ■

Topics in Pain Management CME Quiz

To earn CME credit, you must read the CME article and complete the quiz and evaluation assessment survey on the enclosed form, answering at least 70% of the quiz questions correctly. **Select the best answer and use a blue or black pen to completely fill in the corresponding box on the enclosed answer form.** Please indicate any name and address changes directly on the answer form. If your name and address do not appear on the answer form, please print that information in the blank space at the top left of the page. Make a photocopy of the completed answer form for your own files and mail the original answer form in the enclosed postage-paid business reply envelope. Your answer form must be received by Lippincott CME Institute by **May 31, 2012.** Only two entries will be considered for credit.

Online quiz instructions: To take the quiz online, go to *http://cme.LWWnewsletters.com*, and enter your *username* and *password*. Your *username* will be the letters LWW (case sensitive) followed by the 12-digit account number on your mailing label. You may also find your account number on the paper answer form mailed with your issue. Your *password* will be 1234; this password *may not* be changed. Follow the instructions on the site. You may print your official certificate *immediately*. Please note: Lippincott CME Institute, Inc. *will not* mail certificates to online participants. **Online quizzes expire at 11:59 pm Pacific Standard Time on the due date.**

1. **All of the following statements are true, *except***
   A. The movement of the needle into the muscle normally elicits a brief burst of depolarization from the muscle fibers (termed "insertional activity").
   B. The insertional activity ends immediately upon termination of the movement, with the return of electrical silence.
   C. The only place within the muscle that is not electrically silent is the motor end plate.
   D. There is only one type of electrical activity that can be seen in the motor end plate at rest—miniature end-plate potentials.

2. **It is important to recognize that normal aging does not change the NCV.**
   A. True
   B. False

3. **The H-reflex is a sensitive, specific, and quantitative test of sciatic nerve and S1 nerve root function.**
   A. True
   B. False

4. **The F-response is useful in making the diagnosis of all of the following conditions, *except***
   A. root pathology seen in plexopathy and radiculopathy
   B. Guillain–Barré syndrome
   C. CIDP
   D. occipital neuralgia

5. **Only the gastrocnemius and soleus muscles produce H-reflexes that are reliable enough to be clinically useful.**
   A. True
   B. False

6. **All of the following statements are true, *except***
   A. The NCV is normal (about 40–70 m/s) as long as there are some fast-conducting fibers left in the nerve.
   B. A normal nerve conduction does not rule out a peripheral neuropathy.
   C. Demyelinating neuropathies produce marked slowing of the nerve conduction.
   D. Axonal neuropathies may produce some increase in distal latency, but usually the nerve conductions are slightly increased.

7. **Hypothermia of the entire body or hypothermia in a limb can slow NCV.**
   A. True
   B. False

8. **When a muscle becomes denervated, changes in irritability occur within muscle fibers after 3 weeks.**
   A. True
   B. False

9. **In the case of thoracic outlet syndrome, focal slowing may be detected because of nerve compression, which initially causes a demyelinating lesion.**
   A. True
   B. False

10. **EMG/NCV testing can identify a specific subtype as equivalent to CRPS type 2 (causalgia).**
    A. True
    B. False

NEWS IN BRIEF

A Cruel Adverse Effect of Opioids

A report in the *New York Times* highlights a highly unusual adverse effect of the heavy medical use of opioids in the treatment of chronic pain in the United States.

Katie Zezima and Abby Goodnough pointed out that increasing numbers of workers on long-term, medically prescribed opioid therapy are losing their jobs after failing drug tests. Their employers apparently do not trust individuals taking long-term opioids to function adequately in modern workplaces.

The warnings on opioid package inserts that they "may impair the mental and physical abilities needed to perform potentially hazardous activities" seem to be coming back to haunt those who opt for opioid therapy.

This is no small problem.

According to the *Times* article, the rate of testing positive for opioids among US workers rose 40% from 2005 to 2009. Pain specialists point out that carefully prescribed and supervised opioid therapy should not have a significant deleterious effect on mental or physical performance at work, and that some employees may be losing their jobs without any justification. However, it is also possible that employers can not distinguish individuals on legitimate long-term opioid therapy from those abusing opioids via "doctor shopping" and other forms of drug diversion.

This would seem to be a thorny problem for employers and employees alike. Better scientific evidence about the benefits and risks of opioids, and the indications for their use, would certainly be helpful in sorting through these issues. (*New York Times*, October 4, 2010; www.nytimes.com/2010/10/25/us/25drugs.html.) ■

Physicians Lax in Monitoring Opioids

Despite huge problems with the misuse and abuse of opioids in the management of chronic noncancer pain, primary care physicians in the United States still do not appear to be monitoring opioid use carefully. This provides ammunition for those who would further regulate the use of these powerful medications.

The latest evidence on the lax management of opioids comes fromYeshiva University in New York. Johanna Starrels, MD, and colleagues performed a retrospective review of electronic medical records for 1612 patients who had been prescribed an opioid for chronic noncancer pain. They wanted to observe the frequency of three risk-reduction strategies commonly recommended in the management of opioid therapy: (1) urine drug testing; (2) regular office visits (at least once per six months or within 30 days of modifying the opioid treatment program); and/or (3) restrictions on early refills.

The results are sobering. Urine testing was employed in only 8% of patients. Even among those at high risk of opioid abuse (i.e. those with drug and alcohol abuse disorders and those with mental health problems), only 24% underwent urine testing. Only about half of patients receiving opioids had regular office visits. High-risk cases were no more likely to have regular visits than other patients. Although less than a quarter of patients received two or more early refills, patients at highest risk of opioid-related misuse were most likely to have multiple early refills.

"Our study highlights a missed opportunity for identifying and reducing misuse of prescribed opioids in primary care settings," said lead author Starrels in a published statement from Yeshiva University. "The finding that physicians did not increase precautions for patients at highest risk for opioid misuse should be a call for a standardized approach to monitoring."

It is wise to be cautious in assigning blame for the lack of monitoring of opioid use. Many would hold the treating physicians responsible. However, some of the responsibility may lie with the medical systems in which they work—for not organizing and encouraging risk-reduction strategies. (See Starrels et al. Low use of opioid risk reduction strategies in primary care even for high risk patients with chronic pain. *J Gen Intern Med* 2011; epub ahead of print; doi: 10.1007/s11606-011-1648-2.) ■

Coming Soon:

- Review of Clinical Nerve Function Studies and Imaging, Part II